WHAT IS CLAIMED IS:

1. A method of treating a disease or disorder characterized by high intracellular calcium levels in an individual in need thereof, comprising:

providing an effective amount of an opener of maxi-K potassium channels to said individual, wherein said opener activates maxi-K potassium channels in cells under conditions of high intracellular calcium concentration, and does not significantly activate maxi-K potassium channels in cells under low or normal concentrations of intracellular calcium.

2. The method according to claim 1, further wherein influx or introduction of additional calcium into cells having high intracellular calcium concentration is restricted or reduced.

3. The method according to claim 1, wherein the disease or disorder is a neurodegenerative disease or disorder.

4. The method according to claim 3, wherein the neurodegenerative disease or disorder is selected from the group consisting of stroke, global cerebral ischemia, traumatic brain injury, Parkinson's disease, epilepsy, migraine and Alzheimer's disease.

5. The method according to claim 4, wherein the neurodegenerative disease is stroke.

6. The method according to claim 5, wherein the neurodegenerative disease is ischemic stroke or acute ischemic stroke.

7. The method according to claim 6, wherein the cells having a high intracellular calcium concentration are preischemic or ischemic neurons.

8. The method according to claim 1, wherein the maxi-K potassium channel opener is selected from the group consisting of fluoro-oxindole compounds and chloro-oxindole compounds.

9. The method according to claim 8, wherein the fluoro-oxindole compound is selected from the group consisting of (±)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indol-2-one; (3S)-(+)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indole-2-one; and (3S)-(-)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indole-2-one.

10. The method according to claim 9, wherein the fluoro-oxindole compound is (3S)-(+)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indole-2-one.

11. The method according to claim 8, wherein the chloro-oxindole compound is selected from the group consisting of (±)-3-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-chloro-6-(trifluoromethyl)-2H-indol-2-one; (3S)-(+)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-chloro-6-(trifluoromethyl)-2H-indol-2-one; and (3R)-(-)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-chloro-6-(trifluoromethyl)-2H-indol-2-one.

12. The method according to claim 1, wherein the maxi-K potassium channel opener is administered prior to or following the onset of the disease or disorder.

13. The method according to claim 5 or claim 6, wherein the maxi-K potassium channel opener is administered prior to or following the onset of stroke, ischemic stroke, or acute ischemic stroke.

14. A method of treating stroke in an individual in need thereof, comprising:

administering to the individual an effective amount of a maxi-K channel opener, said opener having opener activity on maxi-K potassium channel proteins in neuronal cells having a high intracellular calcium concentration, while having no significant opener activity on maxi-K potassium channel proteins in neuronal cells having normal or low intracellular calcium concentration.

15. The method according to claim 14, wherein the maxi-K channel opener is selected from the group consisting of fluoro-oxindole compounds and chloro-oxindole compounds.

16. The method according to claim 15, wherein the fluoro-oxindole compound is selected from the group consisting of (±)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indol-2-one; (3S)-(+)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indole-2-one; and (3S)-(-)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indole-2-one.

17. The method according to claim 16, wherein the fluoro-oxindole compound is (3S)-(+)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indole-2-one.

18. The method according to claim 15, wherein the chloro-oxindole compound is selected from the group consisting of (±)-3-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-chloro-6-(trifluoromethyl)-2H-indol-2-one; (3S)-(+)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-chloro-6-(trifluoromethyl)-2H-indol-2-one; and (3R)-(-)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-chloro-6-(trifluoromethyl)-2H-indol-2-one.

19. The method according to claim 14, wherein ischemic stroke or acute ischemic stroke is treated.

20. The method according to claim 14 or claim 19, wherein the maxi-K channel opener is administered prior to or following the onset of stroke, ischemic stroke or acute ischemic stroke.

21. The method according to claim 14, wherein the maxi-K channel opener provides cortical neuroprotection by restricting entry of calcium into neuronal cells exposed to toxic levels of calcium.

22. A method of treating a disease or disorder characterized by high intracellular calcium levels in an individual in need thereof, comprising:

a) providing to the individual an opener of maxi-K channels wherein the opener is sensitive to high intracellular calcium concentration and targets maxi-K channels in cells associated with the disease or disorder and having high intracellular calcium concentration, while not significantly targeting cells having low or normal intracellular calcium concentration; and

b) reducing or restricting influx of additional calcium into the cells associated with the disease or disorder, increasing potassium efflux and regulating membrane potential, thereby protecting the cells associated with the disease or disorder from toxicity or death.

23. The method according to claim 22, wherein the maxi-K channel opener is a fluoro-oxindole compound or a chloro-oxindole compound.

24. The method according to claim 23, wherein the fluoro-oxindole compound is selected from the group consisting of (±)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indol-2-one; (3S)-(+)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-

(trifluoromethyl)-2H-indole-2-one; and (3S)-(-)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indole-2-one.

25. The method according to claim 24, wherein the fluoro-oxindole compound is (3S)-(+)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indole-2-one.

26. The method according to claim 24, wherein the fluoro-oxindole compound is (3S)-(-)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indole-2-one.

27. The method according to claim 23, wherein the chloro-oxindole compound is selected from the group consisting of (±)-3-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-chloro-6-(trifluoromethyl)-2H-indol-2-one; (3S)-(+)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-chloro-6-(trifluoromethyl)-2H-indol-2-one; and (3R)-(-)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-chloro-6-(trifluoromethyl)-2H-indol-2-one.

28. The method according to claim 22, wherein the disease or disorder is a neurodegenerative disease or disorder.

29. The method according to claim 28, wherein the neurodegenerative disease or disorder is selected from the group consisting of stroke, global cerebral ischemia, traumatic brain injury, Parkinson's disease, epilepsy, migraine and Alzheimer's disease.

30. The method according to claim 29, wherein the neurodegenerative disease or disorder is stroke.

31. The method according to claim 30, wherein the neurodegenerative disease or disorder is ischemic stroke or acute ischemic stroke.

32. The method according to claim 22, wherein the cells associated with the disease or disorder and having a high intracellular calcium concentration are at-risk preischemic neurons or ischemic neurons.

33. The method according to claim 29, wherein the neurodegenerative disease or disorder is traumatic brain injury.

34. The method according to claim 22, wherein the maxi-K channel opener is administered prior to or after the onset of the disease or disorder.

35. A method of providing neuroprotection from stroke in an individual in need thereof, comprising: administering an effective amount of a maxi-K potassium channel opener compound that activates maxi-K potassium channel proteins in neurons having a high intracellular calcium concentration, while having no significant opener activity on maxi-K potassium channel proteins in neurons having low or normal intracellular calcium concentration.

36. A method of providing neuroprotection from stroke in an individual in need thereof, comprising: administering an effective amount of a fluoro-oxindole or chloro-oxindole compound to the individual wherein the compound is a maxi-K potassium channel opener compound that activates maxi-K potassium channel proteins in neurons having a high intracellular calcium concentration, while having no significant opener activity on maxi-K potassium channel proteins in neurons having low or normal intracellular calcium concentration, thereby providing cortical neuroprotection by restricting entry of calcium into the neurons at risk for neurotoxicity or death.

37. The method according to claim 35 or claim 36, wherein the maxi-K channel opener compound is a fluoro-oxindole compound.

38. The method according to claim 37, wherein the fluoro-oxindole compound is selected from the group consisting of (±)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indol-2-one; (3S)-(+)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indole-2-one; and (3S)-(-)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indole-2-one.

39. The method according to claim 38, wherein the fluoro-oxindole compound is (3S)-(+)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indole-2-one.

40. The method according to claim 38, wherein the fluoro-oxindole compound is (3S)-(-)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indole-2-one.

41. The method according to claim 35 or claim 36, wherein the maxi-K channel opener compound is a chloro-oxindole compound.

42. The method according to claim 41, wherein the chloro-oxindole compound is selected from the group consisting of (±)-3-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-chloro-6-(trifluoromethyl)-2H-indol-2-one; (3S)-(+)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-chloro-6-(trifluoromethyl)-2H-indol-2-one; and (3R)-(-)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-chloro-6-(trifluoromethyl)-2H-indol-2-one.

43. The method according to claim 35 or claim 36, wherein the maxi-K channel opener compound is administered prior to or after the onset of stroke.

44. The method according to claim 35 or claim 36, wherein the neuroprotection is for ischemic stroke or acute ischemic stroke.

45. The method according to claim 35 or claim 36, wherein the neurons having high intracellular calcium concentration are preischemic and/or ischemic neurons.

46. A method of screening for or identifying opener or agonist compounds capable of activating maxi-K potassium channel proteins under conditions of high intracellular calcium concentration, while not significantly activating maxi-K channel proteins under conditions of normal physiological or low intracellular calcium concentration comprising:

a) contacting a test compound with a maxi-K potassium channel protein-expressing cell under conditions of high intracellular calcium concentration; and

b) selecting as said opener or agonist compounds those test compounds which activate maxi-K potassium channel proteins in the cells under conditions of high intracellular calcium concentration, and which do not significantly activate maxi-K potassium channel proteins in cells under low to normal physiological intracellular calcium concentration.

47. The method according to claim 46, wherein the cells having high intracellular calcium concentration are mammalian cells transfected with cloned maxi-K potassium channel protein-encoding DNA, wherein the maxi-K channel protein is expressed.

48. The method according to claim 46, wherein conditions of high intracellular calcium concentration comprise a calcium concentration in the range of greater than about 250 nanomolar to about 10 micromolar $[Ca^{2+}]_i$.

49. The method according to claim 46, wherein the cells under low or normal physiological intracellular calcium concentration are *Xenopus* oocytes transfected with maxi-K channel protein-encoding DNA, wherein the transfected oocytes express the maxi-K channel protein.

50. The method according to claim 46, wherein conditions of low to normal physiological intracellular calcium concentration comprise a

calcium concentration in the range of about 5 nanomolar to 250 nanomolar $[Ca^{2+}]_i$.

51. The method according to claim 46, wherein activation of the maxi-K channels in cells by the test compound is determined using patch-clamp analysis.

52. The method according to claim 51, wherein the patch-clamp analysis is selected from the group consisting of inside-out excised patch, outside-out excised patch, cell-attached excised patch and whole-cell clamp patch.

53. The method according to claim 52, wherein the patch-clamp analysis is whole-cell clamp patch.

54. The method according to claim 46, wherein activation of maxi-K channel proteins comprises increase or activation of maxi-K channel outward currents after introduction of the test compound.

55. A method of assaying for compounds to identify calcium-sensitive opener compounds which selectively activate maxi-K potassium channel proteins under conditions of high intracellular calcium concentration and which do not significantly activate maxi-K potassium channel proteins under conditions of low intracellular calcium concentration or normal intracellular calcium concentration, comprising:

(a) contacting a maxi-K potassium channel protein with a test compound under conditions of high intracellular calcium concentration; and

(b) determining if the opener compound selectively activates the maxi-K potassium channel protein in the presence of high intracellular calcium concentration, and does not significantly activate the maxi-K potassium channel protein in the presence of low or physiologically normal intracellular calcium concentration.

56. The method according to claim 55, further comprising a positive control which is a maxi-K potassium channel opener compound having the characteristics of being sensitive to high intracellular calcium

concentration and selectively targeting cellular maxi-K potassium channels under conditions of high intracellular calcium concentration.

57. The method according to claim 56, wherein the positive control is a fluoro-oxindole or a chloro-oxindole maxi-K potassium channel opener compound.

58. The method according to claim 57, wherein the positive control is a fluoro-oxindole maxi-K potassium channel opener compound selected from the group consisting of (±)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indol-2-one; (3S)-(+)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indole-2-one; and (3S)-(-)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indole-2-one.

59. The method according to claim 57, wherein the positive control is a chloro-oxindole maxi-K potassium channel opener compound selected from the group consisting of (±)-3-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-chloro-6-(trifluoromethyl)-2H-indol-2-one; (3S)-(+)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-chloro-6-(trifluoromethyl)-2H-indol-2-one; and (3R)-(-)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-chloro-6-(trifluoromethyl)-2H-indol-2-one.

60. A maxi-K opener compound selected or identified according to the method of claim 46 or claim 55.

61. A maxi-K potassium channel opener compound characterized by opening or activating maxi-K potassium channels in cells under conditions of high intracellular calcium concentration, and not significantly opening or activating maxi-K potassium channels in cells under low or normal concentrations of intracellular calcium, wherein said maxi-K opener

compound reduces or restricts influx or introduction of additional calcium into cells under conditions of high intracellular calcium concentration.

62. A compound which is (±)-3-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-chloro-6-(trifluoromethyl)-2H-indol-2-one.

63. A compound which is (3S)-(+)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-chloro-6-(trifluoromethyl)-2H-indol-2-one.

64. A compound which is (3R)-(-)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-chloro-6-(trifluoromethyl)-2H-indol-2-one.

65. A pharmaceutical composition comprising the compound according to any one of claims 62 to 64, and a physiologically acceptable diluent, carrier, or excipient.